Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page: 2

LISTING OF THE CLAIMS:

1. (Previously Presented) A method for controlling the operation of a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:

- (a) providing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, each provided micro-droplet processing request comprising two or more actuator processing requests, each specifying performing at least one action associated with at least one passage of the MF device, the micro-droplet processing requests comprising at least one of:
- (i) creating one or more new micro-droplets at selected stable positions, or
- (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
 - (iv) mixing one or more micro-droplets the actuator processing requests comprising:
- (i) providing a gas pressure in a selected passage by an internal component configured to heat a gas to generate a gas pressure;
- (ii) determining, utilizing at least one internal component, the presence or absence of a micro-droplet at a selected position;
- (iii) after determining the presence or absence of the microdroplet, determining reaction products of one or more components of the microdroplet, if the microdroplet was determined to be present; and
- (b) generating control signals, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page: 3

micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device.

- 2. (Currently amended) The method of claim 1 wherein the control signals comprise electrical [[and]] or optical signals.
- 3. (Original) The method of claim 1 wherein the MF device further comprises external control signals responsive to sensors internal to the MF device, and wherein the step of generating control signals further comprises:
- (a) sensing control signals responsive to one or more internal MF device sensors; and
- (b) adjusting the generated signals that are provided to the MF device in response to the sensed signals so that the performance of a micro-droplet command can be monitored.
- 4. (Currently amended) The method of claim 1 wherein the step of creating [[a]] one or more new micro-droplet micro-droplets further comprises separating one of the one or more new micro-droplet micro-droplets from a fluid aliquot in a metered fashion.
- 5. (Currently amended) The method of claim 1 wherein the step of creating [[a]] one or more new micro-droplets micro-droplets further comprises separating one of the one or more new micro-droplets from a source of fluid loaded into the MF device device, in a metered fashion. fashion.
- 6. (Currently amended) The method of claim 1 wherein the step of moving [[a]] one or more micro-droplet micro-droplets further comprises applying a force on [[the]] one or more micro-droplet micro-droplets active to move [[the]] a micro-droplet from the current stable position to the next selected stable position.

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page: 4

7. (Original) The method of claim 6 wherein the step of applying a force further comprises generating a gas pressure acting on the micro-droplet.

- 8. (Original) The method of claim 1 wherein the step for combining two or more micro-droplets further comprises moving the micro-droplets into adjacency at the selected stable position.
- 9. (Original) The method of claim 1 wherein the step of mixing a micro-droplet further comprises moving the micro-droplet with sufficient speed to result in mixing.

10. (Previously Presented) The method of claim 1

wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device to function together to perform the requested action.

- 11. (Previously Presented) The method of claim 10 wherein the actuator processing requests comprise:
- (i) opening or closing a selected controlled passage by internal components acting as a controllable valve, or
- (ii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by at least one internal component configured to determine a thermal capacity, or
- (iii) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor.

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page: 5

12. (Original) The method of claim 11 wherein the step of opening or closing a controlled passage further comprises melting at least one aliquot of a meltable material, wherein the aliquot of the material is positionable for occluding the controlled passage.

13. (Currently Amended) The method of claim 1 wherein the step of providing a gas pressure in a passage further comprises heating at least [[on]] one gas micro reservoir communicating with the passage.

14. (Canceled)

- 15. (Original) The method of claim 11 wherein the step of sensing the composition of a micro-droplet further comprises sending optical signals to the MF device and receiving optical signals returned from the MF device.
- 16. (Currently amended) The method of claim 11 wherein <u>a</u> request for creating a new micro-droplet from a fluid aliquot in a passage further comprises:
- (i) one or more actuator processing requests to close the passage in order to prevent the fluid aliquot from moving in a reverse direction along the passage, and
- (ii) one or more actuator processing requests to provide controllable gas pressure in order to pinch a new micro-droplet from the fluid aliquot in a metered manner and to propel the new micro-droplet [[to]] in a forward direction to the selected position.
- 17. (Currently amended) The method of claim 11 wherein <u>a</u> request for moving one or more new micro-droplets in a passage further comprises:
- (i) one or more actuator processing requests to close the passage in order to prevent the fluid aliquot from moving in a reverse direction along the passage, and
- (ii) one or more actuator processing requests to provide controllable gas pressure in order to propel the micro-droplet [[to]] in a forward direction to the next stable position.
 - 18. (Currently amended) The method of claim 1 further comprising:

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page: 6

(a) before the step of providing [[a]] <u>one or more</u> micro-droplet processing requests, requests, providing a micro-droplet processing program, wherein a micro-droplet processing program comprises one or more micro-droplet processing requests, and wherein the step of providing [[a]] <u>one or more</u> micro-droplet processing requests further comprises selecting an indicated request from the provided program, and

- (b) repeating the steps of providing [[a]] one or more micro-droplet processing request requests and generating control signals with each micro-droplet processing request until the provided program indicates that no further requests are available for selection.
- 19. (Currently amended) The method of claim 18 wherein the micro-droplet processing program comprises micro-droplet processing requests (i) for creating at least one initial micro-droplet from at least one fluid source, and (ii) for creating at least one final micro-droplet from the at least one initial micro-droplets. micro-droplets.
- 20. (Currently amended) The method of claim 17 further comprising, after the step of creating one or more additional new micro-droplets, a step of detecting contents of certain of the additional new micro-droplets.
- 21. (Original) The method of claim 1 wherein the internal components comprise heaters for applying spatially and temporally localized heating to the MF device, and wherein the control signals comprise electrical signals for activating the localized heaters.
- 22. (Original) The method of claim 21 wherein the internal components comprise at least one aliquot of a meltable material arranged interior to a passage, and wherein the aliquot of material is associated with a heater for melting the material.
- 23. (Currently amended) The method of claim 21 wherein the internal components comprise at least one gas micro reservoir, reservoir having a gas, and wherein the gas micro reservoir is associated with a heater for heating the gas to generate an increased pressure.

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 7

24. (Original) The method of claim 21 wherein the internal components comprise at least one temperature sensor that sense a local temperature of the MF device, and wherein the control signals include signals generated by the temperature sensor.

- 25. (Currently amended) The method of claim 21 wherein at least one temperature sensor is associated with a heater heater, for sensing the sensing localized heating of the MF device by the heater.
- 26. (Currently Amended) A method for controlling the operation of a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:
- (a) providing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either
- (i) creating one or more new micro-droplets at selected stable positions, or
- (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
 - (iv) mixing one or more micro-droplets,

wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,

wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device, and wherein the actuator processing requests comprise,

(i) opening or closing a selected controlled passage by internal components acting as a controllable valve by melting at least one aliquot of a meltable

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page: 8

material, wherein the aliquot of the material is positionable for occluding the controlled passage,

- (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator by heating at least one gas micro reservoir communicating with the passage
- (iii) sensing the presence or absence of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor by sensing an indicator of the thermal capacity in a region about the position, and
- (iv) after sensing the presence of the microdroplet at the selected position, sensing the composition of the micro-droplet at the selected position in the selected passage by internal components acting as a micro-droplet presence sensor by sending optical signals to the MF device and receiving optical signals returned from the [[M'F]] MF device, and
- (b) generating control signals, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device,

wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device to function together to perform the requested action.

27. (Previously Presented) A method for controlling the operation of a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 9

signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:

- (a) providing one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests comprising either
- (i) creating one or more new micro-droplets at selected stable positions by separating the new micro-droplet from an existing micro-droplet or a fluid source in a metered fashion, or
- (ii) moving one or more micro-droplets from current stable positions to selected next stable positions by applying a gas pressure on the micro-droplet active to move the micro-droplet from the current stable position to the next selected stable position, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions by moving the micro-droplets into adjacency at the selected stable position, or
- (iv) mixing one or more micro-droplets by generating control signals for moving the micro-droplet with sufficient speed to result in laminar mixing, wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,

wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device, and wherein the actuator processing requests comprise,

- (i) providing controllable gas pressure in a selected passage by at least one internal component configured to heat a gas to generate a gas pressure, and
- (ii) sensing, utilizing at least one internal component, the presence or absence of a micro-droplet at a first selected position in a selected passage and then determining the presence of a reaction product of at least one component of the microdroplet at a second different position of the microfluidic device if the microdroplet was sensed at the first selected position, and
- (b) generating control signals, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 10

micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device,

wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device to function together to perform the requested action.

- 28. (Previously Presented) A method for performing a chemical reaction in a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:
- (a) providing one or more fluid reagents, wherein the fluid reagents comprise the reactants necessary for the reaction,
- (b) creating at least one final micro-droplet from the fluid reagents by providing control signals to the MF device, wherein the micro-droplet is positioned at a stable position and comprises the reactants necessary for the reaction,
- (c) determining, utilizing at least one internal component, a presence or absence of the at least one final micro-droplet,
- (d) moving the at least one final micro-droplet by heating a gas to generate a gas pressure within the MF device, and
- (e) after the steps of determining, utilizing the at least one internal component, the presence or absence of the at least one final microdroplet and moving the at least one final micro-droplet, reacting the at least one micro-droplets.

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 11

29. (Original) The method of claim 28 wherein the step of reacting further comprises waiting for a time sufficient for occurrence of the reaction.

- 30. (Original) The method of claim 28 wherein the step of reacting further comprises exciting the final micro-droplet by providing control signals to the MF device, wherein the excitation is sufficient to cause occurrence of the reaction.
- 31. (Original) The method of claim 30 wherein the step of exciting comprises thermally heating or optically irradiating the micro-droplet.
- 32. (Original) The method of claim 28 further comprising a step of sensing the composition of the reacted micro-droplet by providing control signals to the MF device.
- 33. (Currently amended) The method of claim 28 wherein the chemical reaction comprises performing [[the]] analysis of a sample.
- 34. (Currently amended) The method of claim 28 wherein the step of creating further comprises:
- (a) providing a micro-droplet processing request, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, the requests request comprising either
- (i) creating one or more new micro-droplets at selected stable positions, or
- (ii) moving one or more micro-droplets from current stable positions to selected next stable positions, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions, or
 - (iv) mixing one or more micro-droplets, and
- (b) generating control signals for each micro-droplet processing request, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each micro-droplet processing request so that the internal

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 12

components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device.

35. (Original) The method of claim 34 further comprising:

- (a) before the step of providing a micro-droplet processing request, providing a micro-droplet processing program, wherein a micro-droplet processing program comprises one or more micro-droplet processing requests, and wherein the step of providing a micro-droplet processing request further comprises selecting an indicated request from the provided program, and
- (b) repeating the steps of providing a request and generating signals with each micro-droplet processing request until the provided program indicates that no further requests are available for selection.
- 36. (Original) The method of claim 34 wherein each provided micro-droplet processing request further comprises one or more actuator processing requests,

wherein an actuator processing request specifies performing at least one action physically associated with at least one passage of the MF device,

wherein the generated pattern and sequence of control signals that is responsive to a micro-droplet processing request further comprises sub-patterns and sub-sequences that are responsive to each actuator processing request of the micro-droplet processing request, and

wherein the sub-pattern and sub-sequence of control signals that is responsive to each actuator processing request cause the responsive internal components of the MF device to function together to perform the requested action.

- 37. (Original) The method of claim 36 wherein the actuator processing requests comprise:
- (i) opening or closing a selected controlled passage by internal components acting as a controllable valve,
- (ii) providing controllable gas pressure in a selected passage by internal components acting as pressure generator,

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 13

(iii) sensing the presence or absence of a micro-droplets at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor, or

- (iv) sensing the composition of a micro-droplet at a selected position in a selected passage by internal components acting as a micro-droplet presence sensor.
- 38. (Previously Presented) A method for performing a chemical reaction in a digital-type microfluidic ("MF") device (i) wherein an MF device comprises one or more passages for confining one or more micro-droplets, the passages having one or more stable positions for the micro-droplets, and (ii) comprises one or more internal components responsive to control signals, the internal components operatively associated with the passages for control and monitoring the MF device, the method comprising:
- (a) providing one or more fluid reagents, wherein the fluid reagents comprise the reactants necessary for the reaction,
- (b) providing a micro-droplet processing program, wherein a micro-droplet processing program comprises one or more micro-droplet processing requests, wherein a micro-droplet processing request specifies performing at least one action on at least one micro-droplet, and the requests comprising either
- (i) creating one or more new micro-droplets at selected stable positions by heating a gas to generate a gas pressure within the MF device, or
- (ii) moving one or more micro-droplets from current stable positions to selected next stable positions by heating a gas to generate a gas pressure within the MF device, or
- (iii) combining two or more micro-droplets into one or more new micro-droplets at selected stable positions by heating a gas to generate a gas pressure within the MF device, or
- (iv) mixing one or more micro-droplets by heating a gas to generate a gas pressure within the MF device,

wherein the micro-droplet processing program provides for the creation of at least one final micro-droplet from the fluid reagents by providing control signals to the MF

Applicant: Kalyan Handique et al.

Serial No.: 09/819,105 Filed: March 28, 2001

Page : 14

device, and wherein the micro-droplet is positioned at a stable position and comprises the reactants necessary for the reaction,

- (c) determining, utilizing at least one internal component, the presence or absence of a micro-droplet within a region of the MF device,
- (d) selecting an indicated micro-droplet processing request from the provided processing program,
- (e) generating control signals for the selected micro-droplet processing request, which are provided to the MF device, wherein the control signals are generated in a pattern and sequence that is responsive to each micro-droplet processing request so that the internal components of the MF device that are responsive to the control signals function together to perform the requested micro-droplet processing in the MF device,
- (f) repeating the steps of providing a request and generating signals with each micro-droplet processing request until the provided program indicates that no further requests are available for selection, and
- (g) reacting the micro-droplet by waiting for a time sufficient for occurrence of the reaction or by exciting the final micro-droplet by providing control signals to the MF device, wherein the excitation is sufficient to cause occurrence of the reaction and where the reacting step is performed after the determining, utilizing the at least one internal component, the presence of the micro-droplet within a region of the MF device.

39-51. (Canceled)

- 52. (Original) A computer readable medium comprising encoded instructions for causing a data acquisition system to perform the method of claim 1.
- 53. (Original) A computer readable medium comprising encoded instructions for causing a data acquisition system to perform the method of claim 26.
- 54. (New) A computer readable medium comprising encoded instructions for causing a data acquisition system to perform the method of claim 27.